Acute Effects of Lung Expansion Maneuvers in Comatose Subjects With Prolonged Bed Rest

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BACKGROUND: Patients with decreased consciousness are prone to prolonged bed rest and respiratory complications. If effective in reducing atelectasis, lung expansion maneuvers could be used to prevent these complications. In comatose, bedridden subjects, we aimed to assess the acute effect on regional lung aeration of 2 lung expansion techniques: expiratory positive airway pressure and the breath-stacking maneuver. Our secondary aim was to evaluate the influence of these lung expansion techniques on regional ventilation distribution, regional ventilation kinetics, respiratory pattern, and cardiovascular system. METHODS: We enrolled 10 subjects status post neurosurgery, unable to follow commands, and with prolonged bed rest. All subjects were submitted to both expansion techniques in a randomized order. Regional lung aeration, ventilation distribution, and regional ventilation kinetics were measured with electrical impedance tomography. RESULTS: Lung aeration increased significantly during the application of both expiratory positive airway pressure and breath-stacking ($P <$ .001) but returned to baseline values seconds afterwards. The posterior lung regions had the largest volume increase ($P <$ .001 for groups). Both maneuvers induced asynchronous inflation and deflation between anterior and posterior lung regions. There were no significant differences in cardiovascular variables. CONCLUSIONS: In comatose subjects with prolonged bed rest, expiratory positive airway pressure and breath-stacking promoted brief increases in lung aeration. (ClinicalTrials.gov registration NCT02613832.) *Key words: physical therapy techniques; positive-pressure respiration; electrical impedance; lung volume measurements.* [Respir Care 2021;66(2):240–247. © 2021 Daedalus Enterprises]

Introduction

Patients with central nervous lesions can develop severe disability or post-coma unresponsiveness that leads to prolonged bed rest.[1] In recent decades, however, there is growing awareness that prolonged bed rest can be deleterious to many organ systems. With regard to the respiratory system, the supine position has been associated with changes in respiratory function such as the reduction of functional residual capacity, tidal volume, and rib cage mobility.[2-4] Furthermore, atelectasis and respiratory infections were described in > 20% of subjects with severe traumatic brain injury.[5]

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Lung expansion maneuvers, such as incentive spirometry, have been routinely applied in clinical situations to prevent respiratory complications and to restore lung function in conditions that induce loss of lung aeration.[6-8] However, these maneuvers require patient cooperation and cannot be applied properly in those who are bedridden because of a decreased level of consciousness. In this scenario, nonvolitional techniques such as the application of expiratory positive airway pressure (EPAP)[9] and the breath-stacking maneuver can be applied.[10] The efficacy and safety of these maneuvers, however, have not been assessed in bedridden subjects.

Our primary aim was to assess the acute effects of both techniques, EPAP and the breath-stacking maneuver, on regional lung aeration in comatose subjects with prolonged bed rest. We also evaluated the impact of the techniques on regional ventilation distribution, regional ventilation kinetics, respiratory pattern, and cardiovascular system.

Methods

This physiologic, randomized, crossover study was conducted in the neurosurgery care unit of a tertiary hospital in Brazil from August 2014 to January 2015. The study was approved by institutional ethics committee (CEP/UFPE: 321.437) and registered on Clinicaltrials.gov (NCT02613832).

Subjects

We included subjects between 18 and 65 y of age who had undergone neurosurgery, were unable to follow commands (Glasgow Coma Scale $\leq$ 10 points), were breathing spontaneously through a tracheostomy tube, and had prolonged bed rest (ie, $>$ 14 d). Written informed consent was obtained from the next of kin. To ensure bed rest was the only risk factor for loss of lung aeration, we excluded patients with chest deformity, rib fracture, asymmetrical chest expansion, moderate spasticity in the upper limbs (Ashworth Scale score $>$ 2), abdominal distention, respiratory infection, or a chronic lung disease.

Study Protocol

Subjects were assessed in a semi-upright sitting position (35°). The tracheostomy tube cuff was inflated with the minimal volume required to avoid air leakage. Endotracheal suction was performed with negative pressure regulated at 100–150 mm Hg. Subjects received CPAP of 10 cm H_2O for 1 min to minimize the effects of endotracheal suction.

The interventions were performed in a randomized order: sequence 1 (breath-stacking followed by EPAP) and sequence 2 (EPAP followed by breath-stacking). After a run-in period of 60 min required to washout the effects of suctioning, subjects were randomized using a series of numbered opaque envelopes. The protocol was interrupted if any of the following occurred: heart rate $<$ 60 or $>$ 120 beats/min; breathing frequency $>$ 35 breaths/min; mean arterial pressure $<$ 60 mm Hg or $>$ 120 mm Hg; or $S_{pO_2} < 90\%$.

QUICK LOOK

Current knowledge

Prolonged bed rest can be deleterious to many organ systems, including changes in respiratory function such as the reduction in functional residual capacity. Lung expansion maneuvers have been applied clinically to prevent respiratory complications, but the efficacy and safety of these maneuvers have not been assessed in bedridden subjects.

What this paper contributes to our knowledge

We investigated the effect of expiratory positive airway pressure and breath-stacking maneuvers on respiratory variables in comatose subjects requiring prolonged bed rest. Expiratory positive airway pressure and breath-stacking increased regional lung aeration, but there was a rapid return to baseline levels shortly thereafter. The maneuvers were associated with heterogeneous and asynchronous ventilation.

Breath-stacking was performed using a T-piece with a 1-way inspiratory valve with its expiratory branch occluded (Fig. 1A). Expiratory occlusion was maintained for 40 s or until we observed a plateau in the lung volume in the electrical impedance tomography (EIT). Three breath-stacking maneuvers were performed with 1-min intervals between them (Fig. 1B). The EPAP was applied with a spring load valve (Vital Signs, Totowa, New Jersey) adjusted to 10 cm H_2O for 5 min. The washout phase was determined when lung aeration returned to baseline values.

Data Acquisition and Analysis

Regional lung aeration, ventilation distribution, and regional ventilation kinetics were assessed using EIT (Enlight 1800, Timpel SA, São Paulo, Brazil). The acquisition was performed with a self-adhesive belt consisting of 32 electrodes positioned around the circumference of the thorax just below the level of the axilla. Pressure and flow signals from a pneumotachograph (Respironics Novametrix, Wallingford, Connecticut) synchronized with the Enlight monitor were recorded to evaluate respiratory pattern. Blood pressure, heart rate, and S_{pO_2} were assessed with a multiparameter monitor DX-2020 (Dixtal Biomedical, São Paulo, Brazil).

Changes in lung aeration were estimated from changes in end-expiratory lung impedance before (baseline), during, and after the maneuvers (at 5, 10, 15, 30, 60, and 300 s)

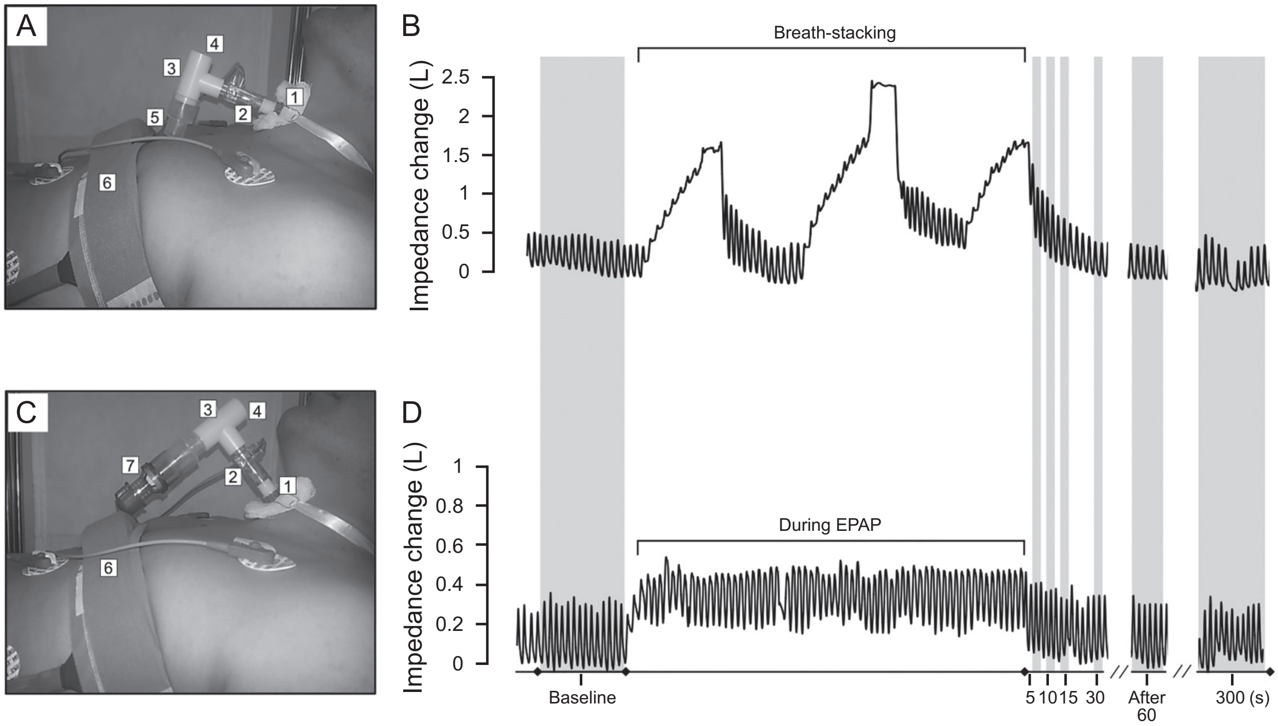

Fig. 1. Illustration of devices used during (A) breath-stacking and (C) expiratory positive airway pressure (EPAP): 1 = tracheostomy tube; 2 = pneumotachograph; 3 = T-piece; 4 = inspiratory branch; 5 = piece to close the expiratory branch; 6 = electrode belt; 7 = spring-loaded valve connected to the expiratory branch. (B, D) Representation of the impedance change before, during, and after the respective maneuvers.

(Figure 1, B and D).[11,12] Changes in end-expiratory lung impedance during the breath-stacking were computed using the mean of the total volume displaced in the 3 maneuvers. Changes in end-expiratory lung impedance were calibrated before the start of the maneuvers against the pneumotachograph and is expressed in liters (see the supplementary materials at http://www.rcjournal.com).[13]

For the ventilation distribution and regional ventilation kinetics, the EIT image was divided into 2 regions of interest (anterior and posterior) with equal height and was processed using a mean of 10 random respiratory cycles before applying a maneuver (ie, quiet breathing) and during the EPAP or breath-stacking maneuver, excluding the first and the last cycles from each step. The cardiovascular variables were recorded before, during, and 60 s and 300 s after the interventions.

Statistical Analysis

Sample size was estimated based on prior data with healthy subjects, who had an average increase in lung aeration of 2.6 L with the same lung expansion techniques.[14] We took a conservative approach to consider a difference that was one third of that found in healthy individuals, considering our target population of comatose subjects, with a resulting standardized effect size of 1.52. The estimated sample size was 10 subjects in each arm, assuming $\alpha = 0.05$ and a power of 80%, using 2-tailed Wilcoxon-Mann-Whitney test (asymptotic relative efficiency method) with software G*Power 3.1 (Heinrich Heine University of Düsseldorf, Germany).

The Shapiro-Wilk test was used to assess normality. Variables are presented as mean ± SD or median and interquartile range when appropriate. Categorical data are presented as absolute values or number and percent of events. The difference between groups at different times was tested using linear mixed models. The P value was considered significant when $< .05$. Previous analyses from these data were presented during a conference.[15] The analyses were performed with the R statistical software (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 57 patients were assessed for eligibility (Figure 2). Table 1 shows the clinical characteristics of the 10 subjects included in the analysis. They had been bedridden for an average length of 21 ± 6.1 d.

Lung Aeration and Cardiovascular Response

Regional lung aeration increased significantly during both maneuvers ($P < .001$ for time, linear mixed model)

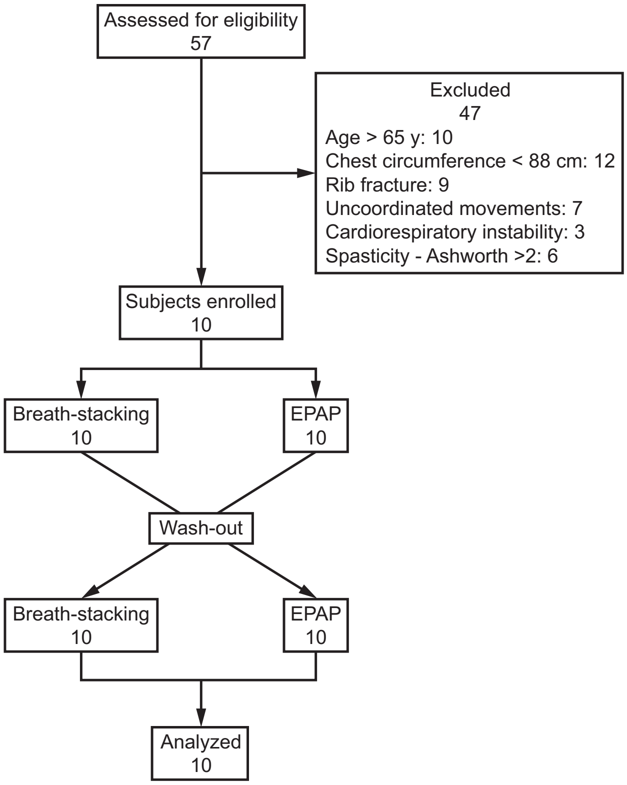

Figure 2. Flow chart.

Table 1. Characteristics of Subjects

Age, y	49.0 ± 16.4
Women	5 (50)
Primary diagnosis	
Stroke	6 (60)
Head injury	3 (30)
Brain tumor	1 (10)
Bed rest, d	21.3 ± 6.1
Predicted weight, kg	66.6 ± 13.7
Glasgow coma scale, median (range)	6 (4–8)
V_T/PBW, mL/kg	5.9 ± 1.4
Breathing frequency, breaths/min	19.3 ± 5.9
Leukocytes, mL/mm^3	9.4 ± 1.9

Data are presented as mean ± SD or *n* (%) unless otherwise noted.
V_T/PBW = tidal volume/predicted body weight

but returned to baseline levels shortly thereafter (Figure 3). The effect on aeration was higher and lasted longer after the breath-stacking maneuver compared to the EPAP maneuver ($P = .005$ for group comparison, linear mixed model) (Figure 3).

No statistical difference was observed in blood pressure, heart rate, or S_{pO_2} compared to baseline values (Table 2).

Effect on Ventilation Distribution and Regional Kinetics

Both maneuvers led to more heterogeneous ventilation compared to baseline. From an even distribution of ventilation during quiet breathing (ie, baseline), ventilation was displaced toward the posterior regions of the lung with the application of EPAP and more so during the breath-stacking maneuver ($P < .001$ for groups, linear mixed model) (Figure 4A).

During quiet breathing, we observed simultaneous inflation and deflation of anterior and posterior regions (Figure 4B). In contrast, during both EPAP and breath-stacking, we found asynchronous inflation and deflation between anterior and posterior lung regions (Figure 4B, from T0 to T1 and from T3 to T4, respectively; see the supplementary materials at http://www.rcjournal.com), an effect that has been termed pendelluft flow.[16]

Expiratory time increased during both maneuvers ($P = .043$ for time, linear mixed model), but the duty cycle (ratio of inspiratory time to total time) did not (Figure 5). Breathing frequency and tidal volume/predicted body weight also increased during both interventions ($P < .001$ for time, linear mixed model).

Discussion

In this study, we evaluated the acute effects of lung expansion maneuvers on lung aeration and ventilation in comatose subjects with prolonged bed rest. During both EPAP and breath-stacking, we noted: (1) regional lung aeration increased significantly, more so during the breath-stacking maneuver, but there was a fast return to baseline levels shortly thereafter; (2) ventilation became more heterogeneous and asynchronous; and (3) there were no adverse cardiovascular events.

The effect of breath-stacking on aeration was 3 times greater than that of EPAP. This finding indicates that our subjects were able to generate considerable inspiratory pressures, sometimes substantially higher than 10 cm H_2O, which was the pressure applied during EPAP (see the supplementary materials at http://www.rcjournal.com). This maneuver, which stacks the inspiratory flow, cycle by cycle, through a 1-way inspiratory valve, was initially described by Marini et al[10] to measure the inspiratory capacity involuntarily and was recently used for lung reexpansion,[17] often achieving higher inspiratory volumes in comparison to standard interventions.[3] Conversely, application of EPAP should increase lung volume in proportion to the pressure imposed during exhalation.[18] However, the effect on lung volume can be attenuated by the action of expiratory muscles, recruited to overcome the expiratory load.[19,20] In a classic study, Van der Schans et al[21] described

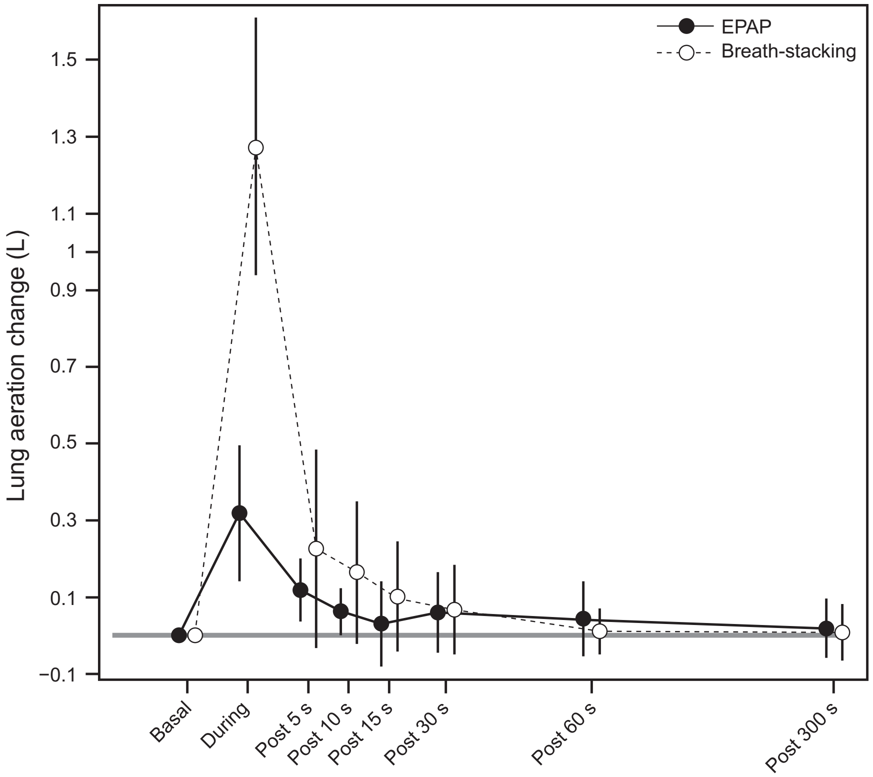

Fig. 3. Regional lung aeration change before (baseline), during, and after breath-stacking and expiratory positive airway pressure (EPAP). $P <$ .001 for group, time, and interaction in a linear mixed model.

no significant change in functional residual capacity with different levels of EPAP.

We also observed a significant increase in the expiratory time during the maneuvers (approximately 15%). This finding suggests that there was indeed abdominal muscle recruitment.[22] During EPAP, half of the expiratory time passed without an effective valve opening (see the supplementary materials at http://www.rcjournal.com; note the constant low expiratory flow), followed by a delayed peak expiratory flow. The breath-stacking maneuver is immune to this recruitment of expiratory muscles due to complete expiratory occlusion.

We observed for the first time the occurrence of heterogeneous ventilation distribution during both maneuvers, with predominant ventilation to the posterior regions. This result can be explained by 2 observations. First, a right-shift on the pressure-volume curve in the anterior region (nondependent) caused by the increase in lung aeration, resulting in regional overinflation and low tidal ventilation.[23,24] In the current study, we observed higher lung impedance in the anterior region of interest during the EPAP and the breath-stacking (Fig. 4B, $P < .001$ for regions of interest), with a consequent reduction in tidal impedance changes (ie, amplitude). Second, we observed pendelluft flow, with the deflation of the anterior region of interest during inspiration, which contributed to $>$ 15% of the total impedance change in the posterior region during the EPAP and in $>$ 40% of the change during the breath-stacking.

The pendelluft flow was originally described as an intrapulmonary asynchrony induced by strong diaphragmatic contraction.[16] In our scenario, we believe that the threshold for opening the 1-way valve and the alveolar PEEP induced by incomplete lung emptying during maneuvers can demand larger inspiratory efforts. Of note, during the breath-stacking maneuver, the pressure swings were sometime on the order of 20–30 cm H_2O (see the supplementary materials at http://www.rcjournal.com).

Immediately after the maneuvers, we observed a significant increase in the breathing frequency and tidal volume (approximately twice the baseline). This response can be explained by a possible increase in CO_2 caused by reduced alveolar ventilation during the breath-stacking (ie, no expired flow until the unidirectional valve is disconnected) and rebreathing expired gas during the EPAP due to the device's dead space ($\sim$ 40 mL). Another possible reason can be related to pendelluft flow, due to the shifted volume composition, considering that the alveolar gas transferred between lung regions is not "fresh" (O_2-poor gas).

No adverse cardiovascular events were observed in this study. Our sample was composed of spontaneously breathing subjects who were clinically stable. These 2 factors may

Table 2. Hemodynamics and Oxygenation Before, During, and After EPAP and Breath-Stacking

Variables / Groups	Before Maneuver	During Maneuver	60 s After Maneuver	300 s After Maneuver	Group Effect, *P*	Time × Group Effect, *P*
Systolic blood pressure, mm Hg						
Expiratory positive airway pressure	137.0 ± 22.1	132.1 ± 22.9	131.2 ± 24.2	138.0 ± 24.7	.40	.99
Breath-stacking	138.8 ± 25.7	137.0 ± 21.0	139.6 ± 22.5	137.0 ± 27.6		
Diastolic blood pressure, mm Hg						
Expiratory positive airway pressure	82.9 ± 12.7	78.3 ± 12.8	78 ± 15.1	86.1 ± 13.4	.10	.22
Breath-stacking	80.8 ± 15.5	89.4 ± 11.2	85.3 ± 9.4	84.3 ± 15.5		
Mean arterial pressure, mm Hg						
Expiratory positive airway pressure	100 ± 13	84 ± 35	72 ± 46	103 ± 15	.26	.86
Breath-stacking	100 ± 17	92.2 ± 39	103 ± 13	95 ± 29		
Heart rate, beats/min						
Expiratory positive airway pressure	103.8 ± 14.3	92.1 ± 38.4	105.3 ± 15.6	107.5 ± 13.9	.19	.45
Breath-stacking	105.3 ± 15.2	109.5 ± 12.9	105.5 ± 12.8	106.3 ± 13.3		
S_{pO_2}, %						
Expiratory positive airway pressure	94.8 ± 2.3	95.9 ± 1.6	96.7 ± 1.5	95.6 ± 3.2	.30	.17
Breath-stacking	96.0 ± 2.1	96.3 ± 2.0	96.6 ± 3.1	96.4 ± 2.6		

Data are presented as mean ± SD obtained from 10 subjects. Statistical significance was accepted at $P < .05$. Differences among interventions at baseline, during, 60 s after the maneuver, and 300 s after the maneuver were tested with general linear model statistics.

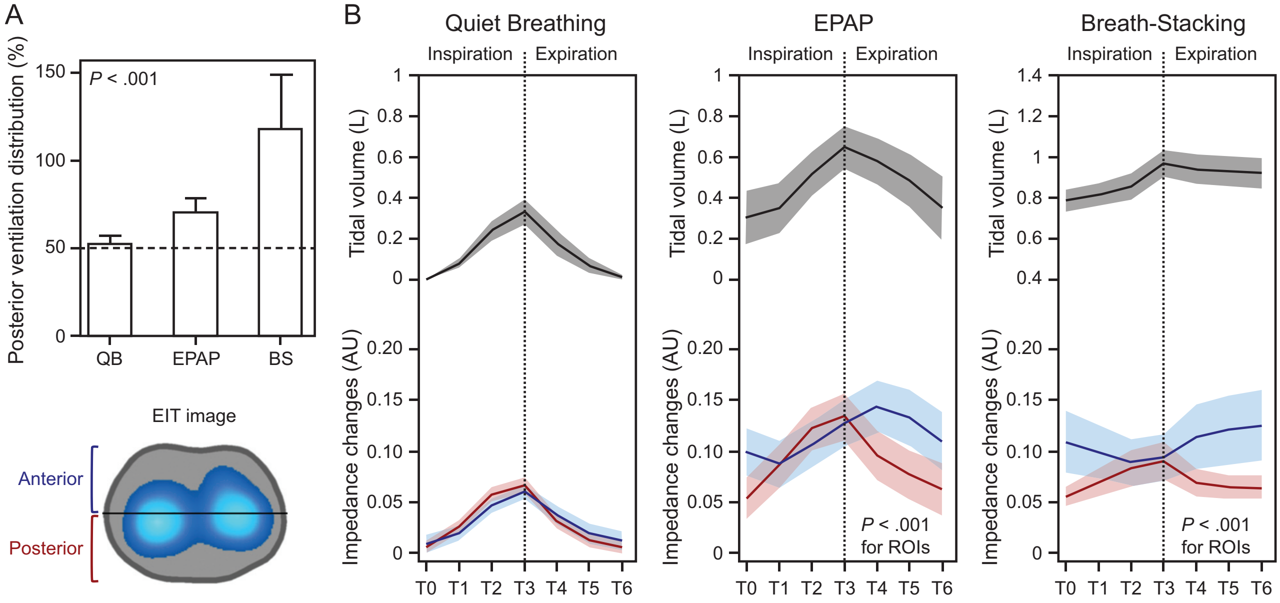

Fig. 4. (A) Posterior ventilation distribution and (B) ventilation kinetics between anterior (blue line) and posterior region of the lung (red line) during quiet breathing (QB), expiratory positive airway pressure (EPAP), and breath-stacking (BS). Note that the ventilation was displaced toward the posterior regions of the lung with the application of the EPAP and the breath-stacking maneuvers. ROI = region of interest.

have contributed to safety during EPAP and breath-stacking, though no other study that used EPAP or breath-stacking reported adverse effects.[3,6-8,10,17]

Finally, this study provides novel physiological information about respiratory maneuvers through EIT monitoring. This noninvasive and bedside device can clinically support individualized chest physiotherapy. Critically analyzing our results, we believe that the undesired respiratory effects outweigh the transient gain in lung aeration in this sample. Possible reasons for the absence of gain after the maneuvers could be the existence of compensatory mechanisms, such as intermittent sighs or a neurological respiratory pattern (ie, Cheyne Stokes) that could re-expand the lung intermittently (see the supplementary materials at http://www.rcjournal.com).

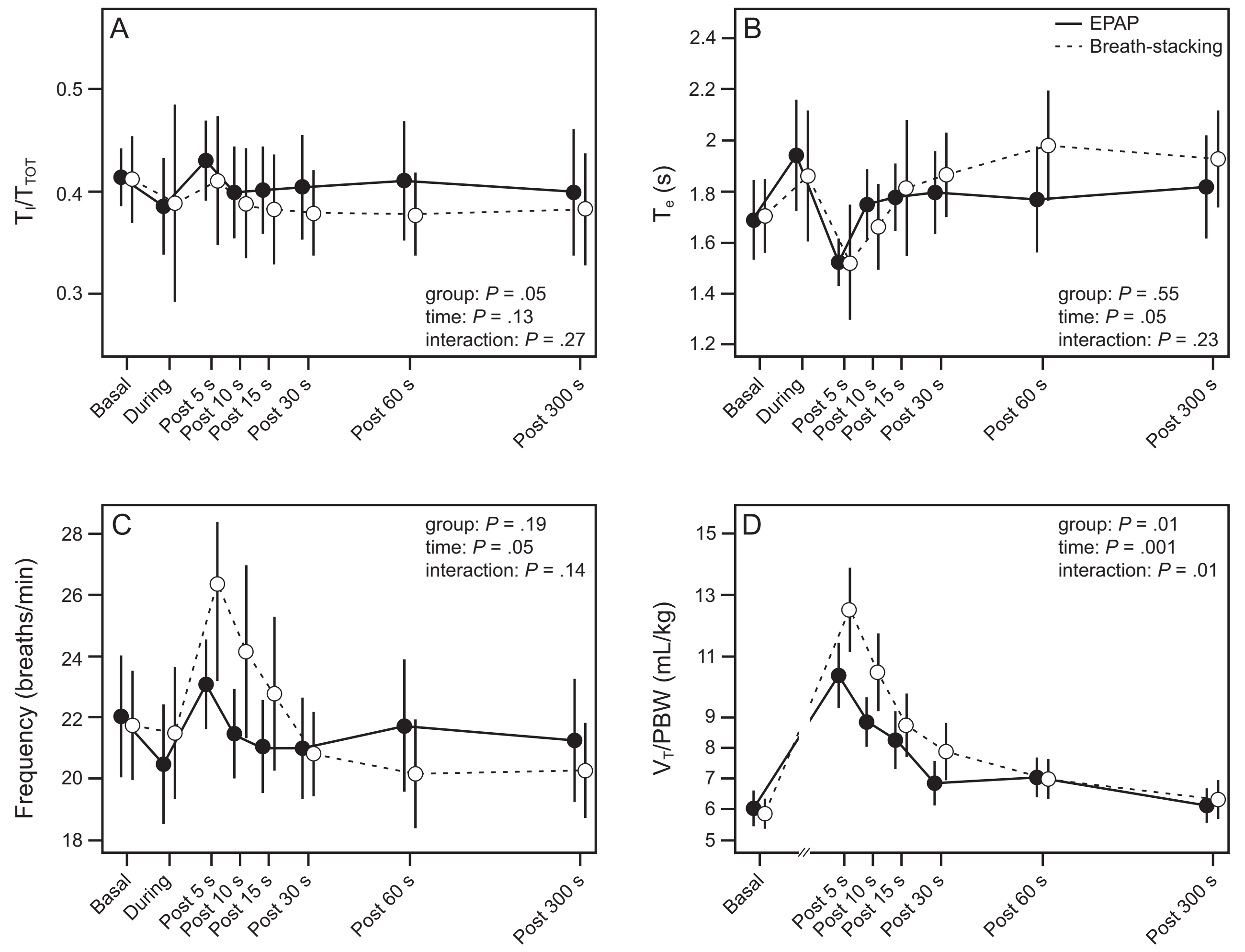

Fig. 5. Respiratory pattern before (baseline), during, and after breath-stacking and expiratory positive airway pressure maneuvers. T_I/T_{TOT} = duty cycle; T_E = expiratory time; V_T/PBW = tidal volume/predicted body weight.

Limitations

This study has several limitations. We decided to study subjects who were completely bedridden for a prolonged time due to an reduced level of consciousness. This limits the generalizability of our findings to other subjects with prolonged bed rest who can still move on their own to some extent. We chose to exclude patients with lung disease, but it is possible that the effect of these maneuvers would be more pronounced in subjects who have lung disease and are more prone to lung collapse. Future studies should also evaluate the effects of these maneuvers in subjects with lung atelectasis and secretions. The effect of the breath-stacking maneuver is likely dependent on the patient's ability to generate inspiratory muscle pressure. We were not able to assess the impact of inspiratory muscle function on these maneuvers because we did not measure maximum inspiratory pressure in our subjects.

Conclusions

In comatose subjects with prolonged bed rest, EPAP and breath-stacking maneuvers promoted transient increases in lung aeration, with a fast return to baseline conditions after the interruption of both maneuvers. The maneuvers were associated with a more dorsal and asynchronous ventilation.

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